



SEQUENCE LISTING

(1) GENERAL INFORMATION

(i) APPLICANT: Wei-Wu He, Kristine K. Kikly, Vishva M. Dixit, Steven M. Ruben

(ii) TITLE OF THE INVENTION: INTERLEUKIN-1 BETA CONVERTING ENZYME LIKE APOPTOSIS PROTEASE-6

(iii) NUMBER OF SEQUENCES: 9

(iv) CORRESPONDENCE ADDRESS:

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- (D) STATE: PA
- (E) COUNTRY: USA
- (F) ZIP: 19406-2799

(v) COMPUTER READABLE FORM:

- (A) MEDIUM TYPE: Diskette
- (B) COMPUTER: IBM Compatible
- (C) OPERATING SYSTEM: DOS
- (D) SOFTWARE: FastSEQ Version 1.5

(vi) CURRENT APPLICATION DATA:

- (A) APPLICATION NUMBER: UNKNOWN
- (B) FILING DATE: HERewith
- (C) CLASSIFICATION:

(vii) PRIOR APPLICATION DATA:

- (A) APPLICATION NUMBER: 60/018,961
- (B) FILING DATE: 05 JUNE 1996

- (A) APPLICATION NUMBER: 60/020,344
- (B) FILING DATE: 23 MAY 1996

- (A) APPLICATION NUMBER: 60/017,949
- (B) FILING DATE: 20 May 1996

(viii) ATTORNEY/AGENT INFORMATION:

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(C) REFERENCE/DOCKET NUMBER: P50483-2

(ix) TELECOMMUNICATION INFORMATION:

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(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 416 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide
(iii) HYPOTHETICAL: NO
(iv) ANTISENSE: NO
(v) FRAGMENT TYPE: N-terminal
(vi) ORIGINAL SOURCE:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

Met	Asp	Glu	Ala	Asp	Arg	Arg	Leu	Leu	Arg	Arg	Cys	Arg	Leu	Arg	Leu	
1				5					10					15		
Val	Glu	Glu	Leu	Gln	Val	Asp	Gln	Leu	Trp	Asp	Val	Leu	Leu	Ser	Arg	
			20					25					30			
Glu	Leu	Phe	Arg	Pro	His	Met	Ile	Glu	Asp	Ile	Gln	Arg	Ala	Gly	Ser	
		35					40					45				
Gly	Ser	Arg	Arg	Asp	Gln	Ala	Arg	Gln	Leu	Ile	Ile	Asp	Leu	Glu	Thr	
		50				55					60					
Arg	Gly	Ser	Gln	Ala	Leu	Pro	Leu	Phe	Ile	Ser	Cys	Leu	Glu	Asp	Thr	
65				70					75					80		
Gly	Gln	Asp	Met	Leu	Ala	Ser	Phe	Leu	Arg	Thr	Asn	Arg	Gln	Ala	Gly	
			85						90					95		
Lys	Leu	Ser	Lys	Pro	Thr	Leu	Glu	Asn	Leu	Thr	Pro	Val	Val	Leu	Arg	
			100						105					110		
Pro	Glu	Ile	Arg	Lys	Pro	Glu	Val	Leu	Arg	Pro	Glu	Thr	Pro	Arg	Pro	
		115					120						125			
Val	Asp	Ile	Gly	Ser	Gly	Gly	Phe	Gly	Asp	Val	Gly	Ala	Leu	Glu	Ser	
		130				135							140			

Leu	Arg	Gly	Asn	Ala	Asp	Leu	Ala	Tyr	Ile	Leu	Ser	Met	Glu	Pro	Cys	
145					150					155					160	
Gly	His	Cys	Leu	Ile	Ile	Asn	Asn	Val	Asn	Phe	Cys	Arg	Glu	Ser	Gly	
			165						170						175	
Leu	Arg	Thr	Arg	Thr	Gly	Ser	Asn	Ile	Asp	Cys	Glu	Lys	Leu	Arg	Arg	
			180					185						190		
Arg	Phe	Ser	Ser	Leu	His	Phe	Met	Val	Glu	Val	Lys	Gly	Asp	Leu	Thr	
		195					200					205				
Ala	Lys	Lys	Met	Val	Leu	Ala	Leu	Leu	Glu	Leu	Ala	Arg	Gln	Asp	His	
	210					215					220					
Gly	Ala	Leu	Asp	Cys	Cys	Val	Val	Val	Ile	Leu	Ser	His	Gly	Cys	Gln	
225				230						235					240	
Ala	Ser	His	Leu	Gln	Phe	Pro	Gly	Ala	Val	Tyr	Gly	Thr	Asp	Gly	Cys	
			245					250						255		
Pro	Val	Ser	Val	Glu	Lys	Ile	Val	Asn	Ile	Phe	Asn	Gly	Thr	Ser	Cys	
		260					265						270			
Pro	Ser	Leu	Gly	Gly	Lys	Pro	Lys	Leu	Phe	Phe	Ile	Gln	Ala	Cys	Gly	
	275					280						285				
Gly	Glu	Gln	Lys	Asp	His	Gly	Phe	Glu	Val	Ala	Ser	Thr	Ser	Pro	Glu	
	290				295					300						
Asp	Glu	Ser	Pro	Gly	Ser	Asn	Pro	Glu	Pro	Asp	Ala	Thr	Pro	Phe	Gln	
305				310					315					320		
Glu	Gly	Leu	Arg	Thr	Phe	Asp	Gln	Leu	Asp	Ala	Ile	Ser	Ser	Leu	Pro	
		325						330						335		
Thr	Pro	Ser	Asp	Ile	Phe	Val	Ser	Tyr	Ser	Thr	Phe	Pro	Gly	Phe	Val	
		340					345					350				
Ser	Trp	Arg	Asp	Pro	Lys	Ser	Gly	Ser	Trp	Tyr	Val	Glu	Thr	Leu	Asp	
	355					360					365					
Asp	Ile	Phe	Glu	Gln	Trp	Ala	His	Ser	Glu	Asp	Leu	Gln	Ser	Leu	Leu	
	370				375					380						
Leu	Arg	Val	Ala	Asn	Ala	Val	Ser	Val	Lys	Gly	Ile	Tyr	Lys	Gln	Met	
385				390					395					400		
Pro	Gly	Cys	Phe	Asn	Phe	Leu	Arg	Lys	Lys	Leu	Phe	Phe	Lys	Thr	Ser	
		405						410					415			

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1578 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTISENSE: NO

(v) FRAGMENT TYPE:

(vi) ORIGINAL SOURCE:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

GCCATGGACG	AAGCGGATCG	GCGGCTCCTG	CGGCGGTGCC	GGCTGCGGCT	GGTGAAGAG	60
CTGCAGGTGG	ACCAGCTCTG	GGACGTCCTG	CTGAGCCGCG	AGCTGTTTCAG	GCCCCATATG	120
ATCGAGGACA	TCCAGCGGGC	AGGCTCTGGA	TCTCGGCGGG	ATCAGGCCAG	GCAGCTGATC	180
ATAGATCTGG	AGACTCGAGG	GAGTCAGGCT	CTTCCTTTGT	TCATCTCCTG	CTTAGAGGAC	240
ACAGGCCAGG	ACATGCTGGC	TTCGTTTCTG	CGAACTAACA	GGCAAGCAGG	AAAGTTGTCG	300
AAGCCAACCC	TAGAAAACCT	TACCCAGTG	GTGCTCAGAC	CAGAGATTCTG	CAAACCAGAG	360
GTTCTCAGAC	CGGAAACACC	CAGACCAGTG	GACATTGGTT	CTGGAGGATT	CGGTGATGTC	420
GGTGCTCTTG	AGAGTTTGAG	GGGAAATGCA	GATTTGGCTT	ACATCCTGAG	CATGGAGCCC	480
TGTGGCCACT	GCCTCATTAT	CAACAATGTG	AACTTCTGCC	GTGAGTCCGG	GCTCCGCACC	540
EGCACTGGCT	CCAACATCGA	CTGTGAGAAG	TTGCGGCGTC	GCTTCTCCTC	GCTGCATTTT	600
ATGGTGGAGG	TGAAGGGCGA	CCTGACTGCC	AAGAAAATGG	TGCTGGCTTT	GCTGGAGCTG	660
GCGCGGCAGG	ACCACGGTGC	TCTGGACTGC	TGCGTGGTGG	TCATTCTCTC	TCACGGCTGT	720
CAGGCCAGCC	ACCTGCAGTT	CCCAGGGGCT	GTCTACGGCA	CAGATGGATG	CCCTGTGTCG	780
GTGAGAAGA	TTGTGAACAT	CTTCAATGGG	ACCAGCTGCC	CCAGCCTGGG	AGGGAAGCCC	840
AAGCTCTTTT	TCATCCAGGC	CTGTGGTGGG	GAGCAGAAAG	ACCATGGGTT	TGAGGTGGCC	900
TCCACTTCCC	CTGAAGACGA	GTCCCCTGGC	AGTAACCCCG	AGCCAGATGC	CACCCCGTTC	960
CAGGAAGGTT	TGAGGACCTT	CGACCAGCTG	GACGCCATAT	CTAGTTTGCC	CACACCCAGT	1020
GACATCTTTG	TGTCCTACTC	TACTTTCCCA	GGTTTTGTTT	CCTGGAGGGA	CCCCAAGAGT	1080
GGCTCCTGGT	ACGTTGAGAC	CCTGGACGAC	ATCTTTGAGC	AGTGGGCTCA	CTCTGAAGAC	1140
CTGCAGTCCC	TCCTGCTTAG	GGTCGCTAAT	GCTGTTTCGG	TGAAAGGGAT	TTATAAACAG	1200
ATGCCTGGTT	GCTTTAATTT	CCTCCGGAAG	AACTTTTCT	TTAAAACATC	ATAAGGCCAG	1260
GGCCCCCTAC	CCTGCCTTAT	CTTGACCCC	AAAGCTTTCC	TGCCCCAGGC	CTGAAAGAGG	1320
CTGAGGCCCTG	GACTTTCCTG	CAACTCAAGG	ACTTTGNAGC	CGGCACAGGG	TCTGCTCTTT	1380
CTCTGCCAGT	GACAGACAGG	CTCTTAGCAG	CTTCCAGATT	GACGACAAGT	GCTGAACAGT	1440
GGAGGAAGAG	GGACAGATGA	ATGCCGTGGA	TTGCACGTGG	NCTCTTGAGC	AGTGGCTGGT	1500
CCAGGGCTAG	TGACTTGGTG	TCCCATGATC	CCTGTGTTGG	TCTCTAGGAG	CAGGGATTAA	1560
CCTCTGCACT	ACTGACAT					1578

(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 639 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO
 (iv) ANTISENSE: NO
 (v) FRAGMENT TYPE:
 (vi) ORIGINAL SOURCE:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

CTGACTGCCA	AGAAAATGGT	GCTGGCTTTG	CTGGAGCTGG	CGCGGCAGGA	CCACGGTGCT	60
CTGGACTGCT	GCGTGGTGGT	CATTCTCTCT	CACGGCTGTC	AGGCCAGCCA	CCTGCAGTTC	120
CCAGGGGCTG	TCTACGGCAC	AGATGGATGC	CCTGTGTCGG	TCGAAAAGAT	TGTGAACATC	180
TTCAATGGGA	CCAGCTGCCC	CAGCCTGGGA	GGGAAGCCCA	AGCTCTTTTT	CATCCAGGCC	240
TGTGGTGGGG	AGCAGAAAGA	CCATGGGTTT	GAGGTGGCCT	CCACTTCCCC	TGAAGACGAG	300
TCCCCTGGCA	GTAACCCCGA	GCCAGATGCC	ACCCCGTTCC	AGGAAGGTTT	GAGGACCTTC	360
GACCAGCTGG	ACGCCATATC	TAGTTTGCCC	ACACCCAGTG	ACATCTTTGT	GTCTTACTCT	420
ACTTTCCCAG	GTTTTGTTTC	CTGGAGGGAC	CCCAAGAGTG	GCTCCTGGTA	CGTTGAGACC	480
CTGGACGACA	TCTTTGAGCA	GTGGGCTCAC	TCTGAAGACC	TGCAGTCCCT	CCTGCTTAGG	540
GTCGCTAATG	CTGTTTCGGT	GAAAGGGATT	TATAAACAGA	TGCCTGGTTG	CTTTAATTTT	600
CTCCGGAAAA	AACTTTTCTT	TTAAAACATC	ATAAGGCAG			639

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 203 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTISENSE: NO

(v) FRAGMENT TYPE: N-terminal

(vi) ORIGINAL SOURCE:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

Met	Val	Leu	Ala	Leu	Leu	Glu	Leu	Ala	Arg	Gln	Asp	His	Gly	Ala	Leu
1				5					10					15	
Asp	Cys	Cys	Val	Val	Val	Ile	Leu	Ser	His	Gly	Cys	Gln	Ala	Ser	His
			20					25						30	
Leu	Gln	Phe	Pro	Gly	Ala	Val	Tyr	Gly	Thr	Asp	Gly	Cys	Pro	Val	Ser
		35					40					45			
Val	Glu	Lys	Ile	Val	Asn	Ile	Phe	Asn	Gly	Thr	Ser	Cys	Pro	Ser	Leu
		50				55						60			
Gly	Gly	Lys	Pro	Lys	Leu	Phe	Phe	Ile	Gln	Ala	Cys	Gly	Gly	Glu	Gln

65		70		75		80									
Lys	Asp	His	Gly	Phe	Glu	Val	Ala	Ser	Thr	Ser	Pro	Glu	Asp	Glu	Ser
			85						90					95	
Pro	Gly	Ser	Asn	Pro	Glu	Pro	Asp	Ala	Thr	Pro	Phe	Gln	Glu	Gly	Leu
			100					105					110		
Arg	Thr	Phe	Asp	Gln	Leu	Asp	Ala	Ile	Ser	Ser	Leu	Pro	Thr	Pro	Ser
		115					120					125			
Asp	Ile	Phe	Val	Ser	Tyr	Ser	Thr	Phe	Pro	Gly	Phe	Val	Ser	Trp	Arg
	130					135				140					
Asp	Pro	Lys	Ser	Gly	Ser	Trp	Tyr	Val	Glu	Thr	Leu	Asp	Asp	Ile	Phe
145				150					155					160	
Glu	Gln	Trp	Ala	His	Ser	Glu	Asp	Leu	Gln	Ser	Leu	Leu	Leu	Arg	Val
			165					170				175			
Ala	Asn	Ala	Val	Ser	Val	Lys	Gly	Ile	Tyr	Lys	Gln	Met	Pro	Gly	Cys
		180				185					190				
Phe	Asn	Phe	Leu	Arg	Lys	Lys	Leu	Phe	Phe	Met					
	195					200									

(2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 34 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTISENSE: NO

(v) FRAGMENT TYPE:

(vi) ORIGINAL SOURCE:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

GAACGGGGTA CCGCCATGGA CGAAGCGGAT CCGC

34

(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 60 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: cDNA
- (iii) HYPOTHETICAL: NO
- (iv) ANTISENSE: NO
- (v) FRAGMENT TYPE:
- (vi) ORIGINAL SOURCE:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

TGCTCTAGAT TAGTGGTGGT GGTGGTGGTG TGATGTTTTA AAGAAAAGTT TTTTCCGGAG

60

(2) INFORMATION FOR SEQ ID NO:7:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 41 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: cDNA
- (iii) HYPOTHETICAL: NO
- (iv) ANTISENSE: NO
- (v) FRAGMENT TYPE:
- (vi) ORIGINAL SOURCE:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

AAGCTCTTTT TCATCCAGGC CGCGGGTGGG GAGCAGAAGA C

41

(2) INFORMATION FOR SEQ ID NO:8:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 39 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: cDNA
- (iii) HYPOTHETICAL: NO
- (iv) ANTISENSE: NO
- (v) FRAGMENT TYPE:
- (vi) ORIGINAL SOURCE:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

GTCTTTCTGC TCCCCACCCG CGGCCTGGAT GAAAAAAGC

39

(2) INFORMATION FOR SEQ ID NO:9:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 66 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: NO

(iv) ANTISENSE: NO

(v) FRAGMENT TYPE:

(vi) ORIGINAL SOURCE:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

TGCTCTAGAT TACTTGTCAT CGTCGTCCTT GTAGTCTGAT GTTTTAAAGT TAAGTTTTTT
CCGGAG

60

66

What is claimed is:

1. An isolated polynucleotide comprising a member selected from the group consisting of:
 - 5 (a) a polynucleotide having at least a 70% identity to a polynucleotide encoding a polypeptide comprising amino acids of SEQ ID NO: 1;
 - (b) a polynucleotide which is complementary to the polynucleotide of (a); and
 - (c) a polynucleotide comprising at least 15 bases of the polynucleotide of
- 10 (a) or (b).
2. The polynucleotide of Claim 1 wherein the polynucleotide is DNA.
3. The polynucleotide of Claim 1 wherein the polynucleotide is RNA.
- 15 4. The polynucleotide of Claim 2 which encodes a polypeptide comprising amino acid set forth in SEQ ID NO: 1.
5. An isolated polynucleotide comprising a member selected from the group consisting of:
 - 20 (a) a polynucleotide having at least a 70% identity to a polynucleotide encoding the same mature polypeptide expressed by the human DNA in SEQ ID NO: 2;
 - (b) a polynucleotide complementary to the polynucleotide of (a); and
 - 25 (c) a polynucleotide comprising at least 15 bases of the polynucleotide of
- (a) or (b).
6. A vector comprising the DNA of Claim 2.
- 30 7. A host cell comprising the vector of Claim 6.

8. A process for producing a polypeptide comprising: expressing from the host cell of Claim 7 a polypeptide encoded by said DNA.

5 9. A process for producing a cell which expresses a polypeptide comprising transforming or transfecting the cell with the vector of Claim 6 such that the cell expresses the polypeptide encoded by the human cDNA contained in the vector.

10 10. A polypeptide comprising an amino acid sequence which is at least 70% identical to amino acid set forth in SEQ ID NO: 1.

11. A polypeptide comprising an amino acid sequence as set forth in SEQ ID NO: 1.

15 12. An agonist to the polypeptide of Claim 10.

13. An antibody against the polypeptide of Claim 10.

20 14. An antagonist which inhibits the activity of the polypeptide of Claim 10.

25 15. A method for the treatment of a patient having need of ICE LAP-6 comprising: administering to the patient a therapeutically effective amount of the polypeptide of Claim 10.

16. The method of Claim 15 wherein said therapeutically effective amount of the polypeptide is administered by providing to the patient DNA encoding said polypeptide and expressing said polypeptide *in vivo*.

17. A method for the treatment of a patient having need to inhibit ICE LAP-6 polypeptide comprising: administering to the patient a therapeutically effective amount of the antagonist of Claim 14.

5 18. A process for diagnosing a disease or a susceptibility to a disease related to expression of the polypeptide of Claim 10 comprising: determining a mutation in the nucleic acid sequence encoding said polypeptide.

10 19. A diagnostic process comprising: analyzing for the presence of the polypeptide of Claim 10 in a sample derived from a host.

20. A method for identifying compounds which bind to and activate or inhibit a receptor for the polypeptide of Claim 10 comprising: contacting a cell expressing on the surface thereof a receptor for the polypeptide, said receptor being
15 associated with a second component capable of providing a detectable signal in response to the binding of a compound to said receptor, with a compound to be screened under conditions to permit binding to the receptor; and determining whether the compound binds to and activates or inhibits the receptor by detecting the presence or absence of a signal generated from the interaction of the compound with the
20 receptor.

ABSTRACT OF THE DISCLOSURE

Human ICE LAP-6 polypeptides and DNA (RNA) encoding such ICE LAP-6 and a procedure for producing such polypeptides by recombinant techniques is disclosed. Also disclosed are methods for utilizing such ICE LAP-6 for the treatment of a susceptibility to viral infection, tumorigenesis and to diseases and defects in the control embryogenesis and tissue homeostasis, and the nucleic acid sequences described above may be employed in an assay for ascertaining such susceptibility. Antagonists against such ICE LAP-6 and their use as a therapeutic to treat Alzheimer's disease, Parkinson's disease, rheumatoid arthritis, septic shock, sepsis, stroke, chronic inflammation, acute inflammation, CNS inflammation, osteoporosis, ischemia reperfusion injury, cell death associated with cardiovascular disease, polycystic kidney disease, apoptosis of endothelial cells in cardiovascular disease, degenerative liver disease, MS, ALS, cererbellar degeneration, ischemic injury, myocardial infarction, AIDS, myelodysplastic syndromes, aplastic anemia, male pattern baldness, and head injury damage are also disclosed. Also disclosed are diagnostic assays for detecting diseases related to mutations in the nucleic acid sequences and altered concentrations of the polypeptides. Also disclosed are diagnostic assays for detecting mutations in the polynucleotides encoding the interleukin-1 beta converting enzyme apoptosis proteases and for detecting altered levels of the polypeptide in a host.